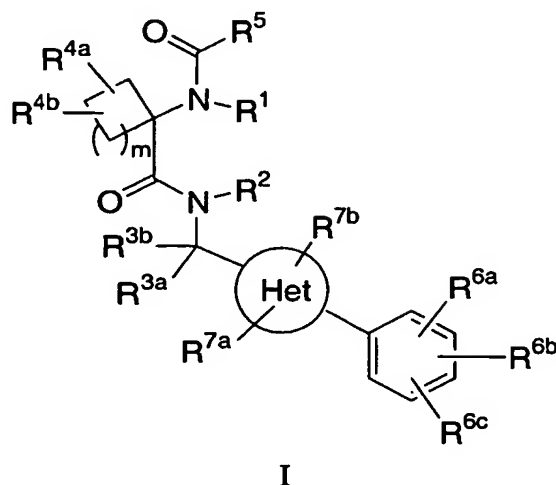


WHAT IS CLAIMED IS:

1. A compound of formula I and pharmaceutically acceptable salts thereof:



wherein

Het is pyrimidinyl or pyridyl, or N-oxide thereof;

R¹ and R² are independently selected from hydrogen and C₁₋₄ alkyl;

- 10 R^{3a} and R^{3b} are independently selected from hydrogen and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms;

R^{4a} and R^{4b} are independently selected from (1) hydrogen, (2) halogen, and (3) C₁₋₄ alkyl optionally substituted with 1 to 4 groups selected from halogen, OR^a, OC(O)R^a, S(O)_kR^d, OS(O)₂R^d, and NR¹R², or

- 15 R^{4a} and R^{4b} together with the carbon atom to which they are both attached form an exo-cyclic methylene optionally substituted with 1 to 2 groups selected from C₁₋₄ alkyl optionally substituted with 1-5 halogen atoms and C₁₋₄ alkyloxy;

R⁵ is selected from (1) C₁₋₆ alkyl optionally substituted with 1 to 5 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, COR^a, SO₂R^d, CO₂R^a, OC(O)R^a, NR^bR^c,

- 20 NR^bC(O)R^a, NR^bC(O)₂R^a, C(O)NR^bR^c, C₃₋₈ cycloalkyl, (2) C₃₋₈ cycloalkyl optionally substituted with 1 to 5 groups independently selected from halogen, nitro, cyano and phenyl, (3) C₃₋₆ alkynyl, (4) C₂₋₆ alkenyl optionally substituted with hydroxyethyl, (5) (CH₂)_k-aryl optionally substituted with 1 to 3 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, C(O)₂R^a, C₁₋₄ alkyl and C₁₋₃ haloalkyl, wherein aryl is selected from phenyl, 3,4-methylenedioxyphenyl and naphthyl, (6) (CH₂)_k-heterocycle optionally substituted with 1 to 3
- 25

- groups independently selected from halogen, nitro, cyano, OR^a, SR^a, C₁₋₄ alkyl and C₁₋₃ halo-alkyl wherein said heterocycle is selected from (a) a 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms wherein said ring is optionally benzo-fused; (b) a 6-membered heteroaromatic ring
- 5 containing from 1 to 3 ring nitrogen atoms and N-oxides thereof, wherein said ring is optionally benzo-fused; and (c) a 5- or 6-membered non-aromatic heterocyclic ring selected from tetrahydrofuranyl, 5-oxotetrahydrofuranyl, 2-oxo-2H-pyranyl, and 6-oxo-1,6-dihydropyridazinyl, (7) C(O)₂R^a, (8) C(O)NR^bR^c, and (9) NR^bCO₂R^a;
- R^{6a} is selected from (1) C₁₋₈ alkyl optionally substituted with 1-5 groups independently selected
- 10 from halogen, nitro, cyano, COR^a, CO₂R^a, C(O)NR^bR^c, OR^a, OC(O)R^a, SR^a, SO₂R^d, S(O)R^d, NR^bR^c, NR^bC(O)R^a, NR^bSO₂R^d, NR^bCO₂R^a, (2) C₃₋₈ cycloalkyl, (3) C₂₋₈ alkenyl optionally substituted with CO₂R^a, (4) halogen, (5) cyano, (6) nitro, (7) NR^bR^c, (8) NR^bC(O)R^a, (9) NR^bCO₂R^a, (10) NR^bC(O)NR^bR^c, (11) NR^bC(O)NR^bCO₂R^a, (12) NR^bSO₂R^d, (13) CO₂R^a, (14) COR^a, (15) C(O)NR^bR^c, (16) C(O)NHO^a, (17) C(=NO^a)R^a, (18) C(=NO^a)NR^bR^c,
- 15 (19) OR^a, (20) OC(O)_kR^a, (21) S(O)_kR^d, (22) SO₂NR^bR^c, and (23) optionally substituted heterocycle where the heterocycle is selected from (a) a 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms, (b) 4,5-dihydro-oxazolyl, and (3) 4,5-dihydro-1,2,4-oxadiazolyl, and wherein said substituent is 1 to 3 groups independently selected from C₁₋₄ alkyl optionally
- 20 substituted with 1 to 5 halogen atoms, OR^a or OC(O)R^a, R^{6b} and R^{6c} are independently selected from hydrogen, and a group from R^{6a}; with the proviso that not more than one of R^{6a}, R^{6b}, and R^{6c} is a heterocycle; R^{7a} and R^{7b} are independently selected from hydrogen, halogen, cyano, nitro, OR^a, CO₂R^a, C(O)NR^bR^c, SO₂R^d, NR^bR^c, and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms;
- 25 R^a is selected from (1) hydrogen, (2) C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, (3) phenyl optionally substituted with 1 to 3 groups independently selected from halogen, cyano, nitro, OH, C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, (4) C₃₋₆ cycloalkyl, and (5) pyridyl;
- R^b and R^c are independently selected from (1) hydrogen, (2) C₁₋₄ alkyl optionally substituted
- 30 with 1 to 5 groups independently selected from halogen, amino, mono-C₁₋₄alkylamino, di-C₁₋₄alkylamino, and SO₂R^d, (3) (CH₂)_k-phenyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, and (4) C₃₋₆ cycloalkyl, or

R^b and R^c together with the nitrogen atom to which they are attached form a 4-, 5-, or 6-membered ring optionally containing an additional heteroatom selected from N, O, and S; or

R^b and R^c together with the nitrogen atom to which they are attached form a cyclic imide;

R^d is selected from (1) C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, (2) C₁₋₄

5 alkyloxy, and (3) phenyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms;

k is 0, 1 or 2; and

m is 0, 1, 2 or 3.

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2. A compound of Claim 1 wherein R⁵ is C₁₋₆ alkyl optionally substituted with 1 to 5 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, COR^a, SO₂R^d, CO₂R^a, OC(O)R^a, NR^bR^c, NR^bC(O)R^a, C(O)NR^bR^c, and C₃₋₈ cycloalkyl, 1,2,5-thiadiazolyl, isoxazolyl, isothiazolyl or pyrimidinyl.

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3. A compound of Claim 1 wherein R⁵ is C₁₋₃ alkyl optionally substituted with 1 to 5 group halogen atoms wherein said halogen is chloro or fluoro.

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4. A compound of Claim 1 wherein R⁵ is selected from difluoromethyl, dichloromethyl, chlorodifluoromethyl, trifluoromethyl, 1,1-dichloroethyl and 2,2,2-trifluoroethyl.

5. A compound of Claim 1 wherein R⁵ is pyrimidinyl.

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6. A compound of Claim 1 wherein R⁵ is 1,2,5-thiadiazolyl, isoxazolyl or isothiazolyl.

7. A compound of Claim 1 wherein R^{6a} is OR^a, CO₂R^a or tetrazolyl optionally substituted with C₁₋₄ alkyl.

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8. A compound of Claim 1 wherein R^{6a} is OR^a, CO₂R^a or tetrazolyl optionally substituted with C₁₋₄ alkyl, R^{6b} is hydrogen or halogen, and R^{6c} is hydrogen or halogen.

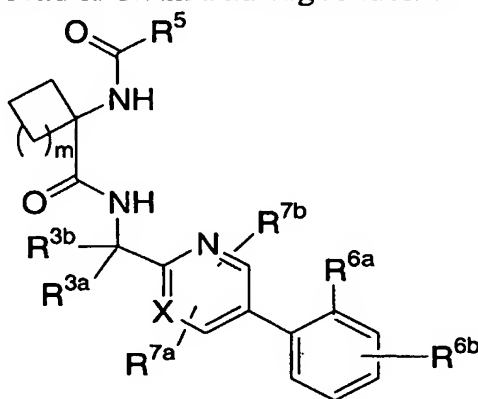
9. A compound of Claim 1 wherein R^{6a} is methoxycarbonyl, ethoxycarbonyl, C₁₋₄alkoxy optionally substituted with 1 to 5 halogen atoms, or 2-methyl-2H-tetrazol-5-yl, R^{6b} is fluoro or chloro, and R^{6c} is hydrogen, chloro or fluoro.

10. A compound of Claim 1 wherein Het is 2,5-pyridinediyl and R^{7a} and R^{7b} are independently hydrogen or halogen.

11. A compound of Claim 10 wherein one of R^{7a} and R^{7b} is hydrogen and the other is fluoro or chloro.

12. A compound of Claim 1 wherein m is 0 or 1.

13. A compound of Claim 1 having formula Ia:



Ia

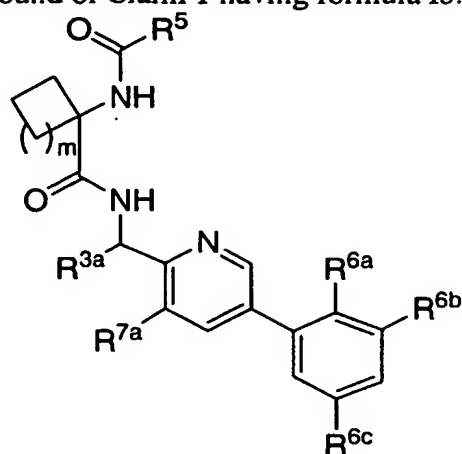
wherein X is carbon or nitrogen, and all other variables are as defined Claim 1.

14. A compound of Claim 13 wherein m is 0 or 1 and one of R^{3a} and R^{3b} is hydrogen and the other is hydrogen or C₁₋₃alkyl.

15. A compound of Claim 13 wherein X is carbon, R^{7a} is hydrogen or chloro or fluoro, and R^{7b} is hydrogen.

16. A compound of Claim 13 wherein X is nitrogen and R^{7a} and R^{7b} are each hydrogen.

17. A compound of Claim 1 having formula Ib:



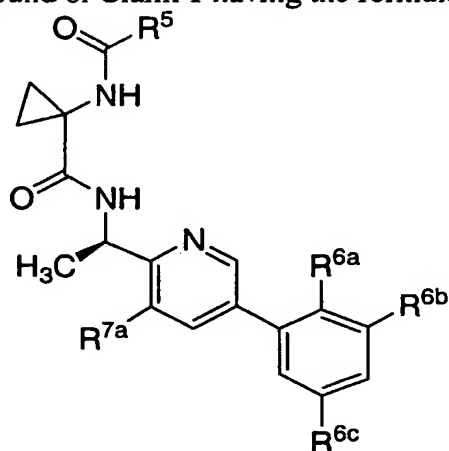
Ib

wherein m is 0 or 1, R^{3a} is hydrogen or methyl, R^{6b} and R^{6c} are independently hydrogen, chloro or fluoro, R^{7a} is hydrogen, chloro or fluoro, and the other variables are as defined in Claim 1.

18. A compound of Claim 17 wherein R^{3a} is hydrogen, and R^{6b} and R^{7a} are each independently chloro or fluoro.

19. A compound of Claim 17 wherein R^{3a} is hydrogen, R^{6b} and R^{7a} are each independently chloro or fluoro, R⁵ is selected from isoxazolyl, thiazolyl, 1,2,5-thiadiazolyl, 5-pyrimidinyl and C₁₋₂alkyl substituted with 1 to 3 halogen atoms selected from chloro and fluoro, and R^{6a} is OR^a, CO₂R^a or 2-methyl-5-tetrazolyl.

20. A compound of Claim 1 having the formula Ic:



Ic

wherein R⁵, R^{6a}, R^{6b}, R^{6c} and R^{7a} are as defined in Claim 1.

21. A compound of Claim 20 wherein R^{6b} is halogen, and R^{6c} and R^{7a} are
5 independently hydrogen or halogen.

22. A compound of Claim 20 wherein R⁵ is selected from isoxazolyl,
isothiazolyl, 1,2,5-thiadiazolyl, 5-pyrimidinyl and C₁₋₂alkyl substituted with 1 to 5 halogen
atoms.

23. A compound of Claim 21 wherein R⁵ is selected from isoxazolyl,
isothiazolyl, 1,2,5-thiadiazolyl, 5-pyrimidinyl and C₁₋₂alkyl substituted with 1 to 5 halogen
atoms.

24. A compound of Claim 20 wherein R^{6a} is selected from CO₂C₁₋₄alkyl,
C₁₋₄alkoxy optionally substituted with 1 to 5 halogen atoms and 2-methyl-5-tetrazolyl.

25. A compound of Claim 23 wherein R^{6a} is selected from CO₂C₁₋₄alkyl,
C₁₋₄alkoxy optionally substituted with 1 to 5 halogen atoms and 2-methyl-5-tetrazolyl.

26. A pharmaceutical composition comprising a therapeutically effective
amount of a compound of Claim 1 and pharmaceutically acceptable excipients.

27. A method of treatment or prevention of pain and inflammation comprising
25 a step of administering, to a subject in need of such treatment or prevention, an effective amount
of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

28. A method of treatment of osteoarthritis, repetitive motion pain, dental
pain, cancer pain, myofascial pain, muscular injury pain, fibromyalgia pain, perioperative pain
30 comprising a step of administering, to a subject in need of such treatment, an effective amount of
a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

29. A method of treatment or prevention of inflammatory pain caused by
chronic obstructive pulmonary disease, asthma, inflammatory bowel disease, rhinitis,

pancreatitis, cystitis (interstitial cystitis), uveitis, inflammatory skin disorders, rheumatoid arthritis, edema resulting from trauma associated with burns, sprains or fracture, postsurgical intervention, osteoarthritis, rheumatic disease, teno-synovitis, or gout comprising a step of administering, to a subject in need of such treatment or prevention, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

30. A method of treatment or prevention of pain associated with angina, menstruation or cancer comprising a step of administering, to a subject in need of such treatment or prevention, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

31. A method of treatment of diabetic vasculopathy, post capillary resistance, diabetic symptoms associated with insulinitis, psoriasis, eczema, spasms of the gastrointestinal tract or uterus, Crohn's disease, ulcerative colitis, or pancreatitis comprising a step of administering, to a subject in need of such treatment, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

32. A method of treatment or prevention of pain caused by pneumoconiosis, including aluminosis, anthracosis, asbestosis, chalicosis, ptilosis, siderosis, silicosis, tabacosis, byssinosis, adult respiratory distress syndrome, bronchitis, allergic rhinitis, vasomotor rhinitis, liver disease, multiple sclerosis, atherosclerosis, Alzheimer's disease, septic shock, cerebral edema, headache, migraine, closed head trauma, irritable bowel syndrome, or nephritis comprising a step of administering, to a subject in need of such treatment or prevention of pain, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.